

FIGURE 1

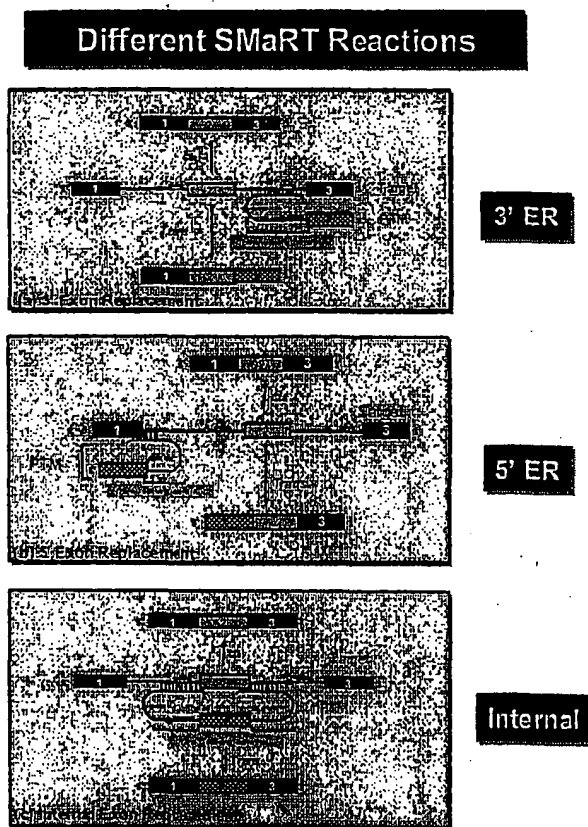
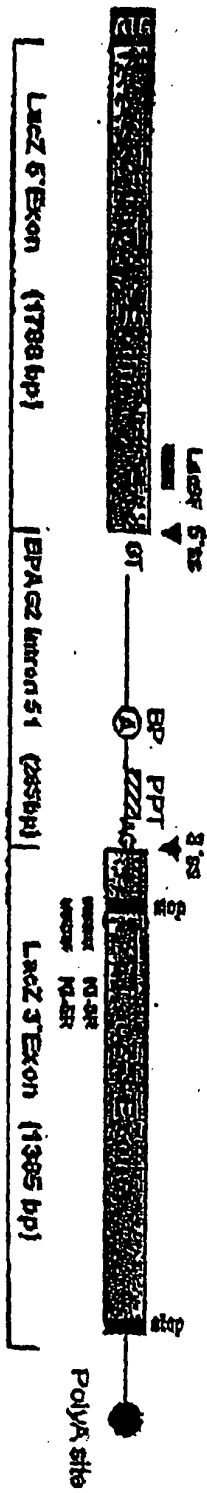


Figure 1. Schematic representation of different SMaRT reactions. (a) *Trans*-splicing reactions between the target 5' splice site and PTMs 3' splice site; (b) *Trans*-splicing reactions between the target 3' splice site and PTMs 5' splice site and (c) Replacement of internal exon by double *trans*-splicing reaction in which the PTM carry both 3' and 5' splice sites. BD, binding domain; BP, branchpoint sequence; PPT, polypyrimidine tract and ss, splice sites.

FIGURE 2A

1) BPAG2 Target 1 (LacZ-T1)



2) BPAG2 Target 2 (T2)

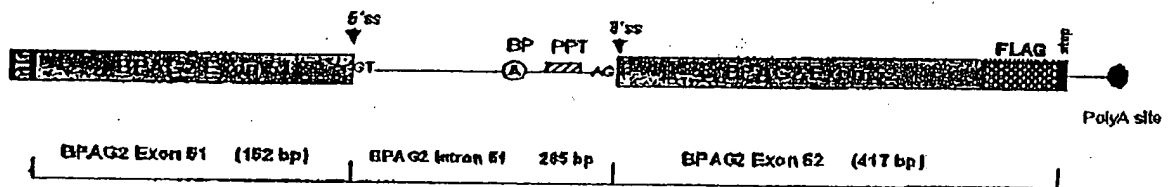


FIGURE 2B

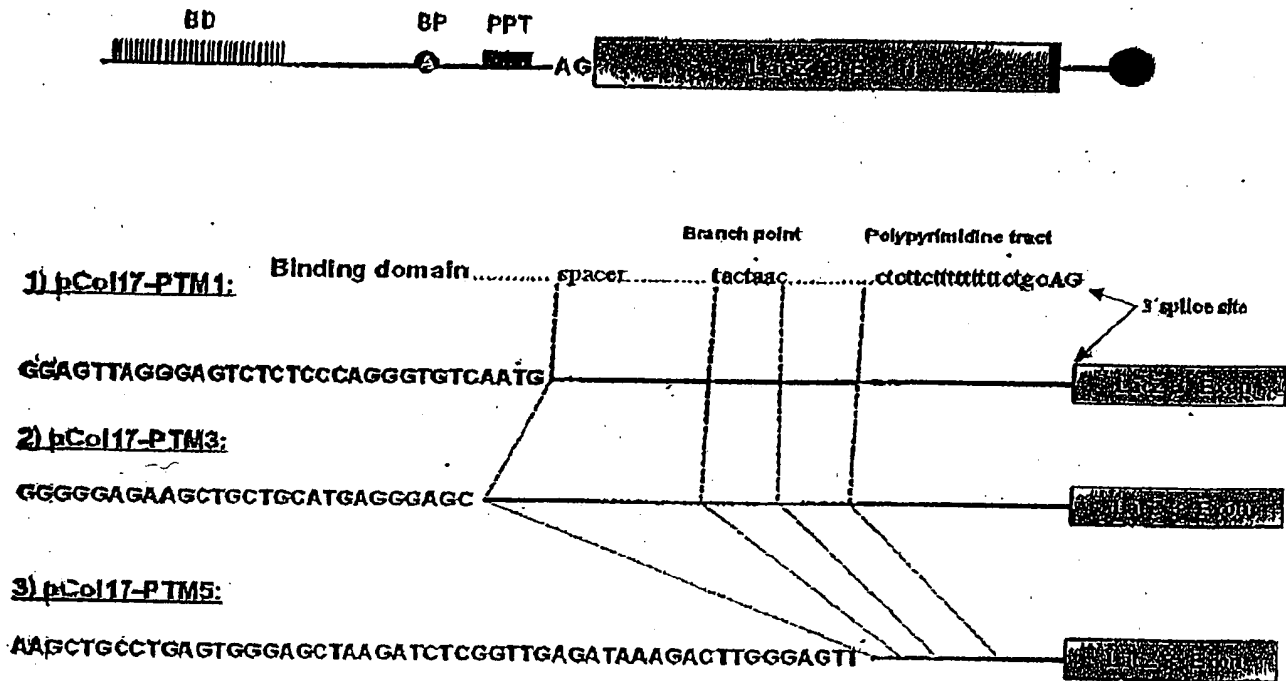


FIGURE 2C

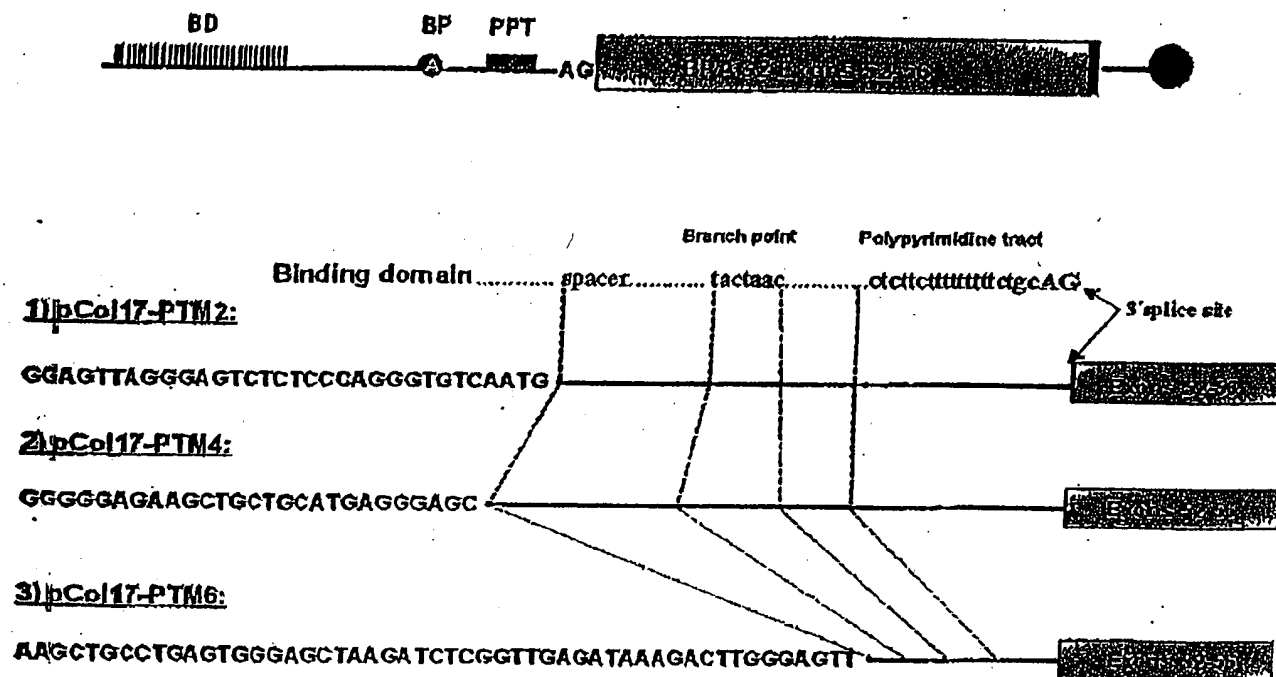
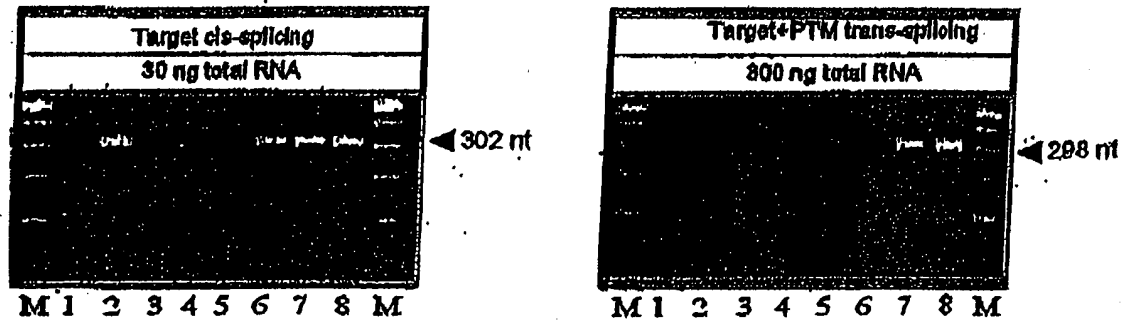


FIGURE 2D

A



B

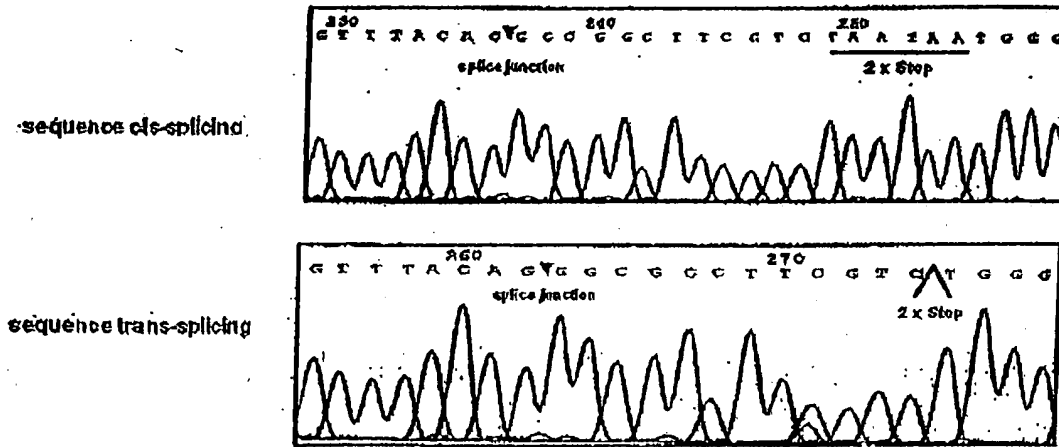


FIGURE 3A-B

Q

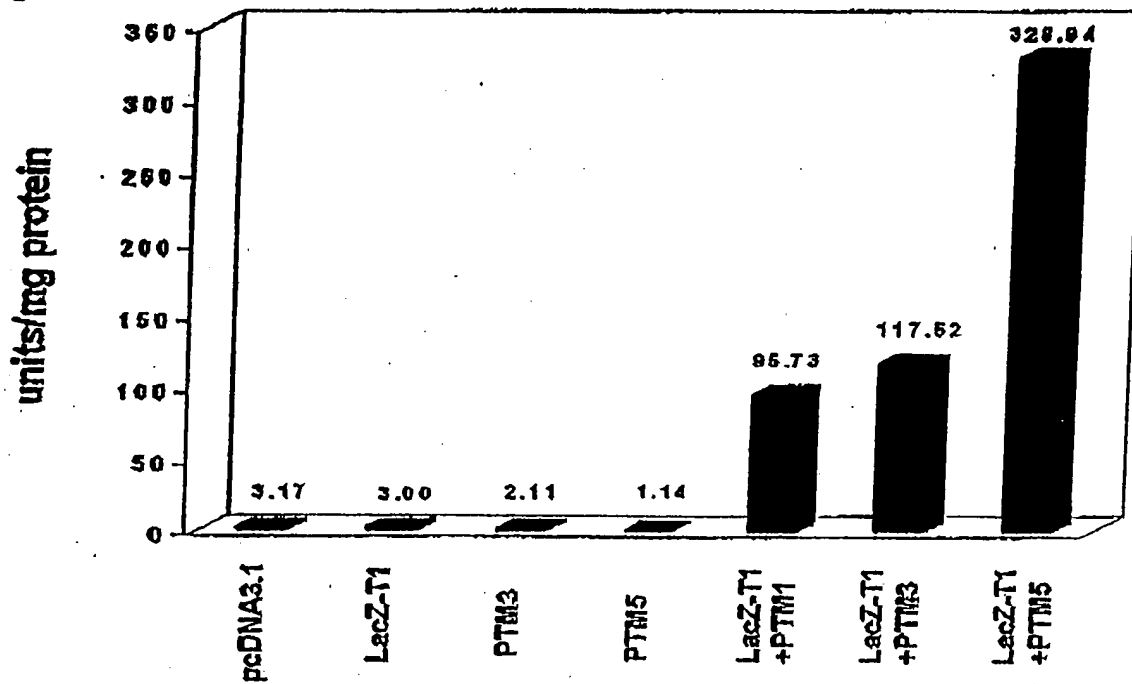


FIGURE 3C

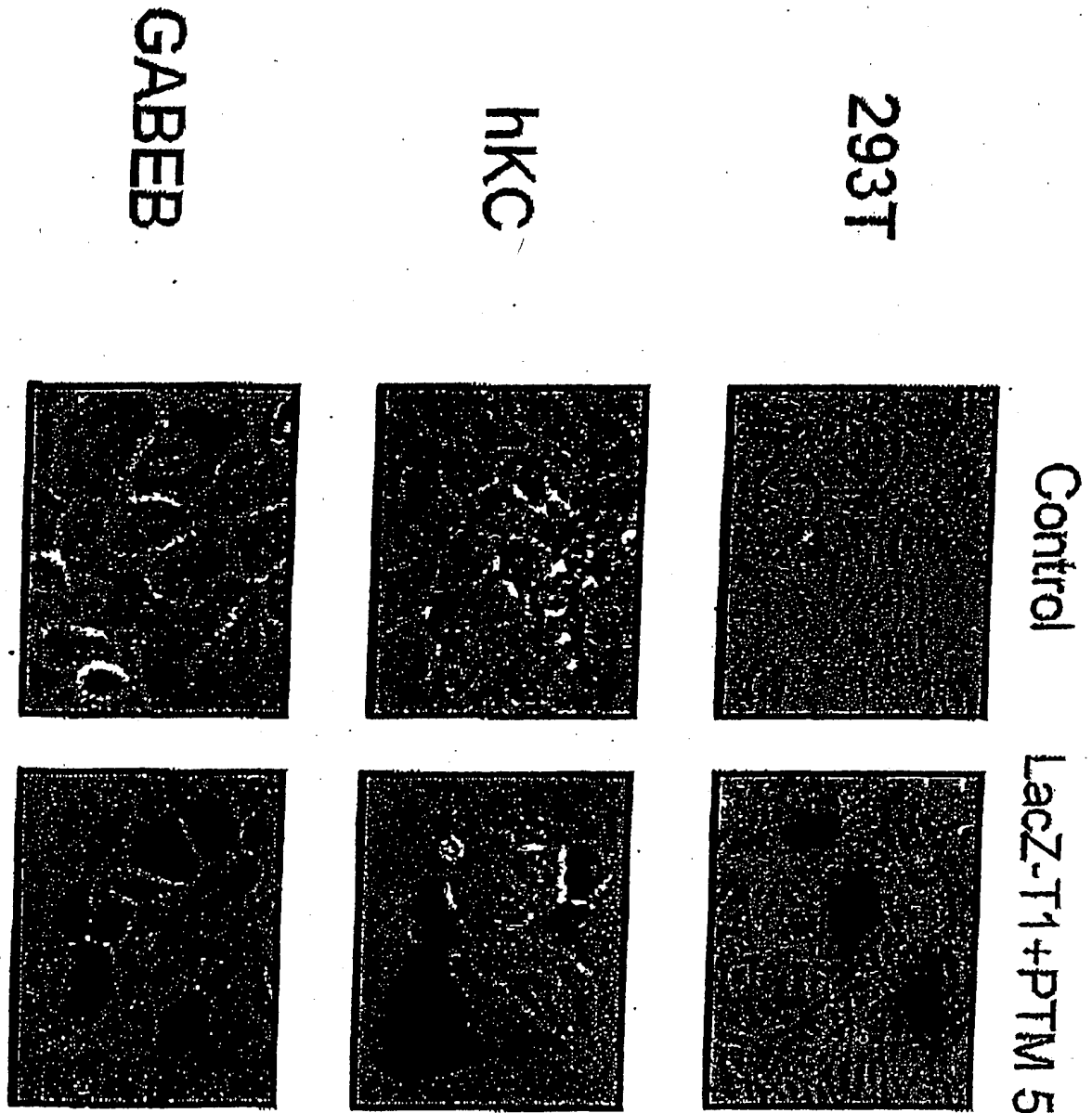
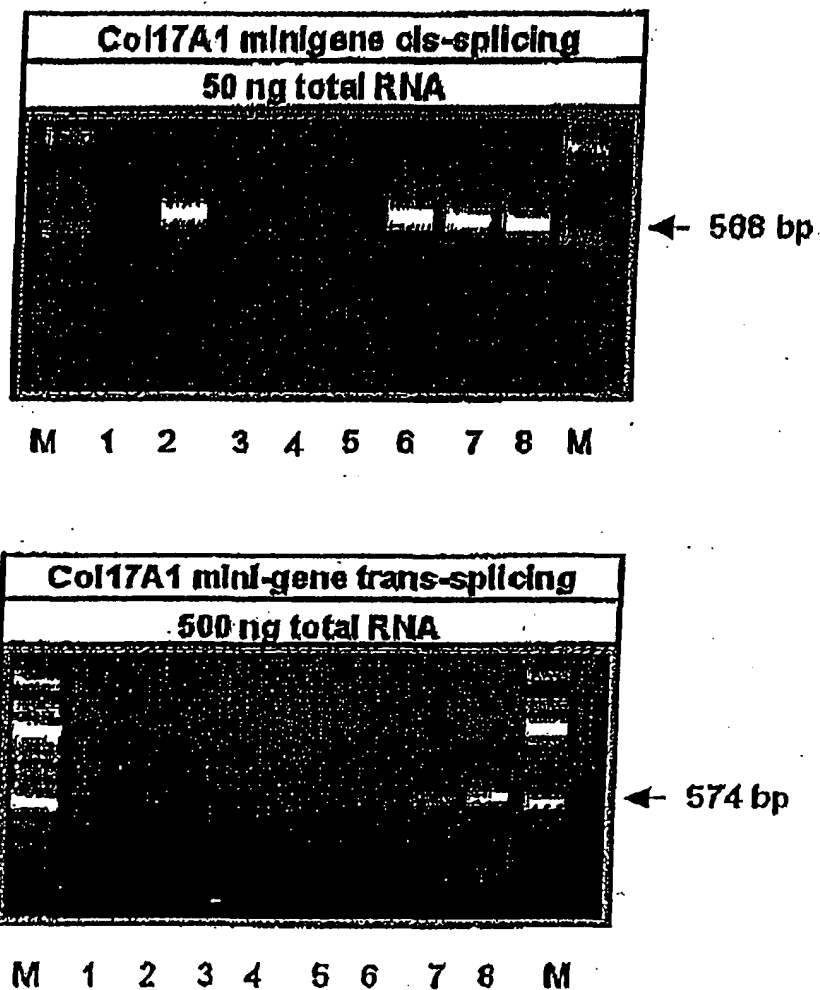


FIGURE 4

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A



B

COL17A1 minigene (T2)

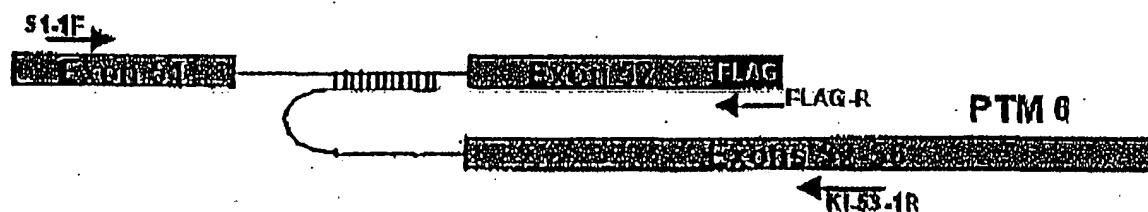


FIGURE 5A-B

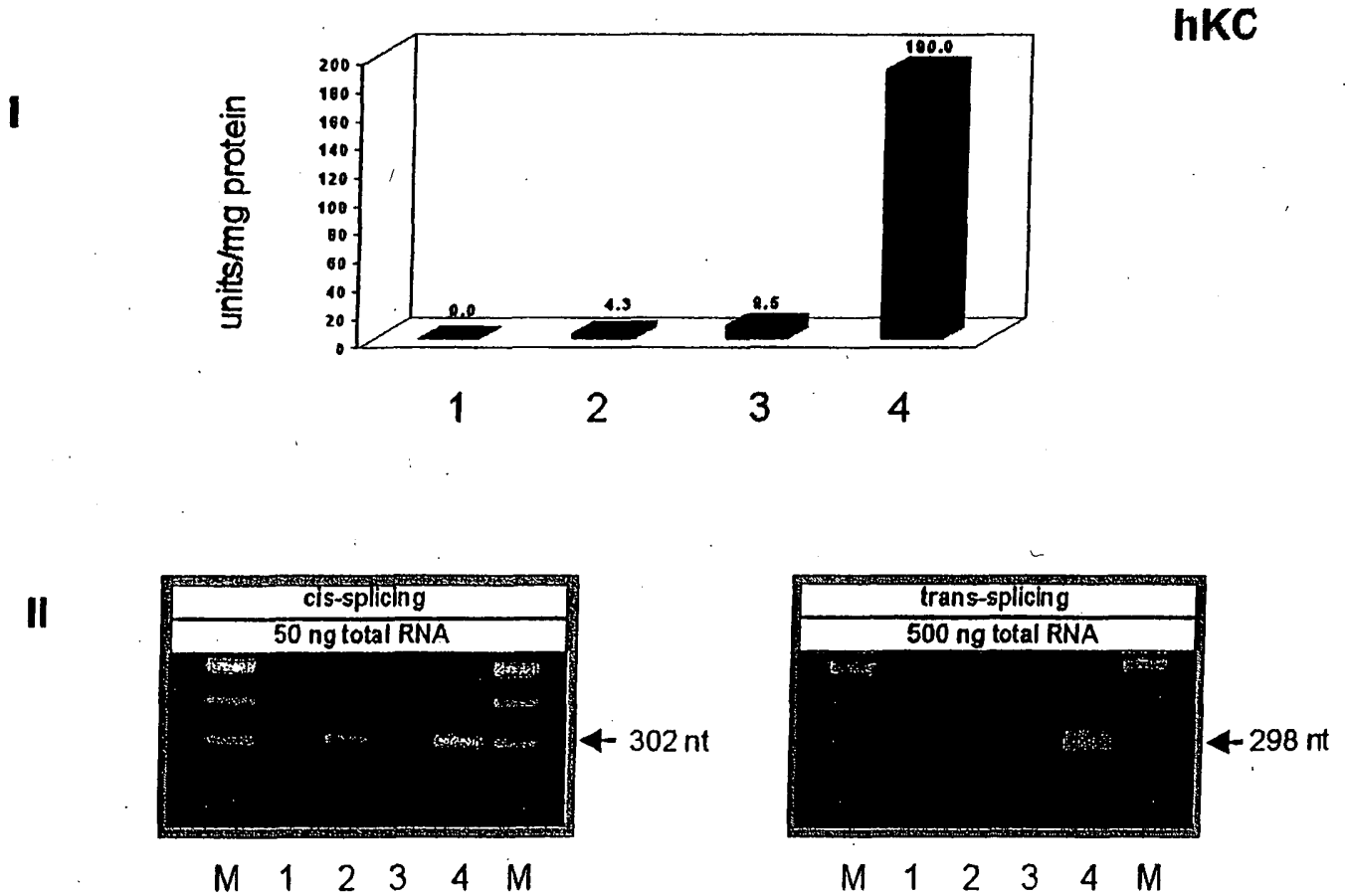


FIGURE 6A

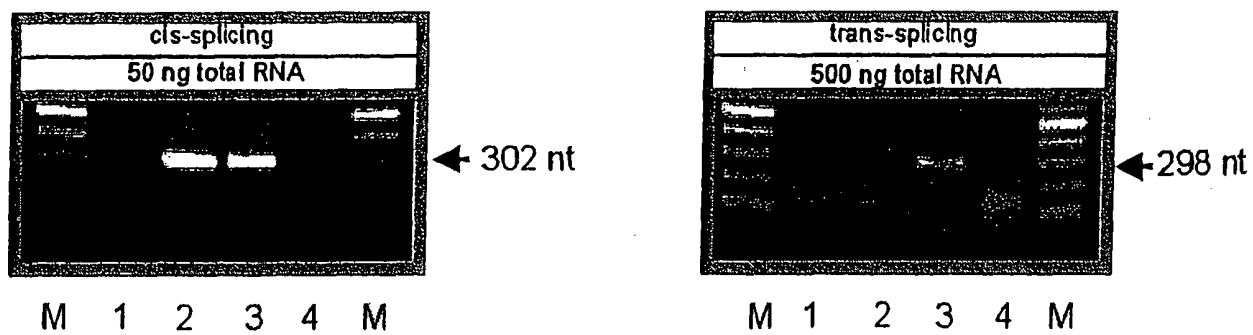
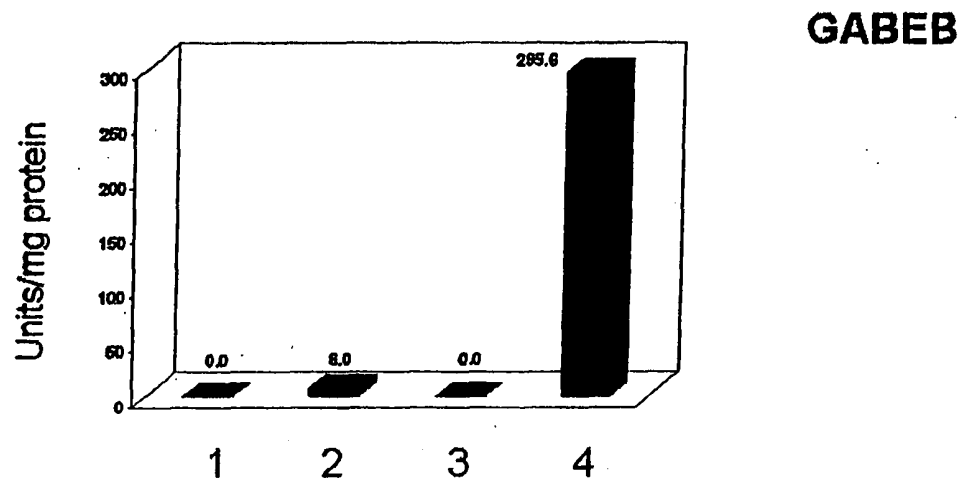


FIGURE 6B

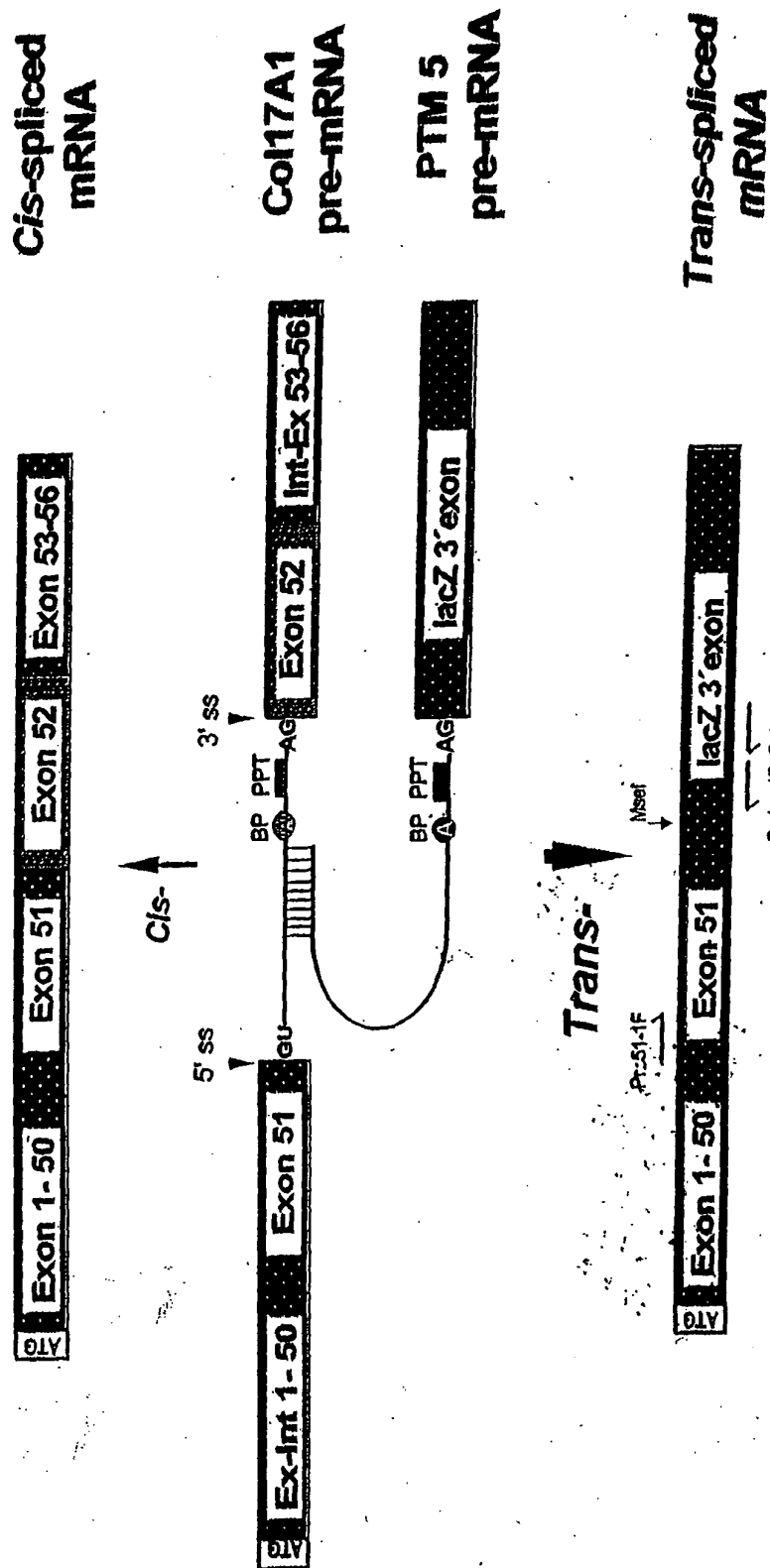
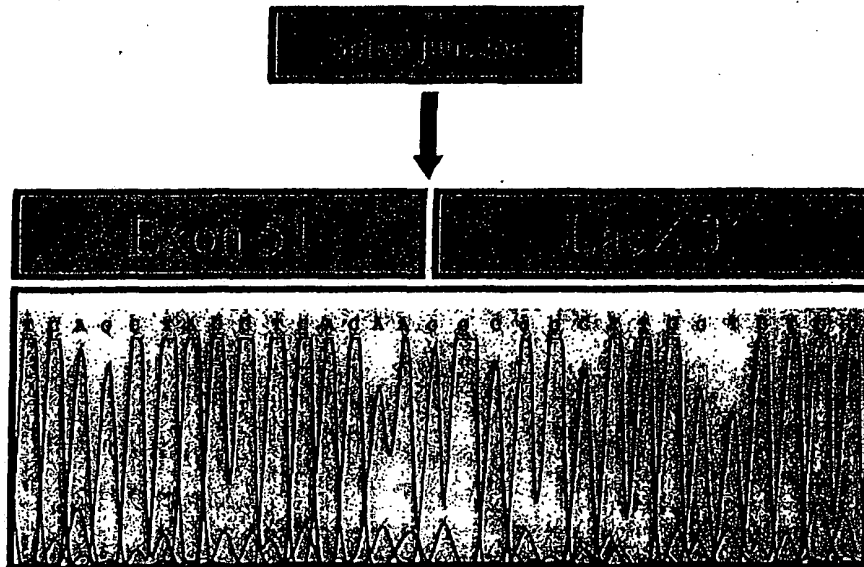


FIGURE 8

Endogenous Transsplicing of Col17 pre-mRNA with PTM5 pre-mRNA

A)



B)

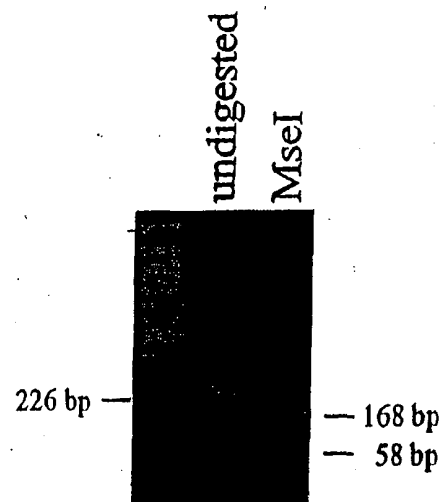


FIGURE 9

5' trans-splicing in a LacZ-model system for hereditary diseases

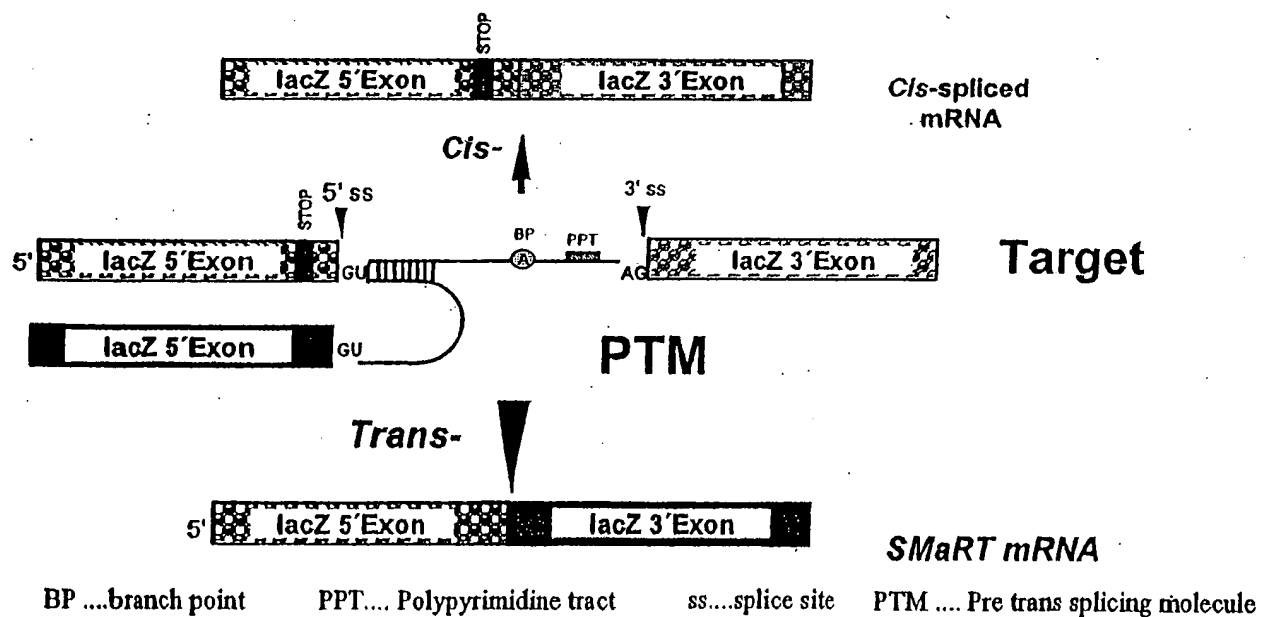


FIGURE 10

Target LacZ-T3 (containing Intron 9) and LacZ-T4 used for optimizing trans-splicing and transfection conditions

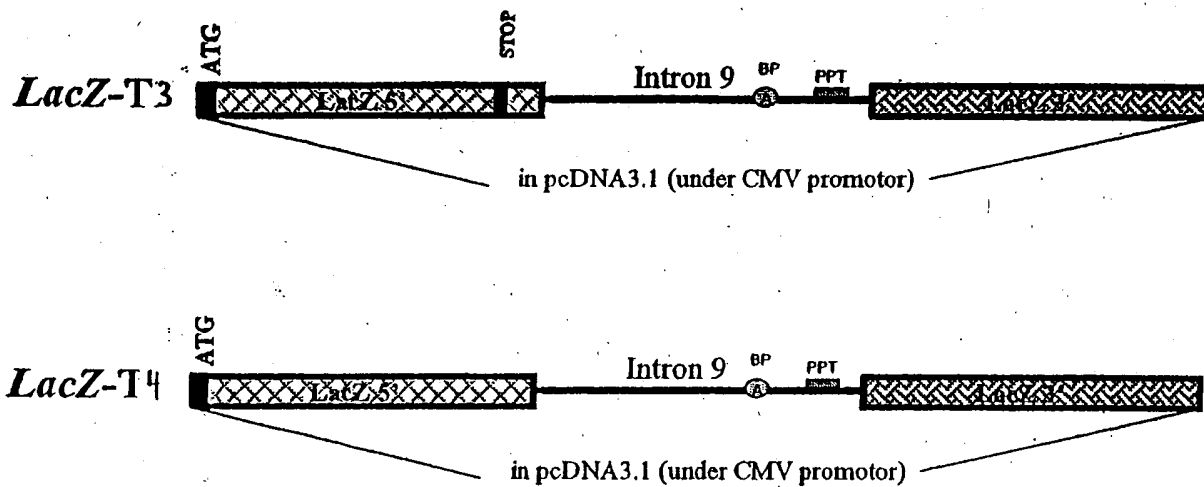
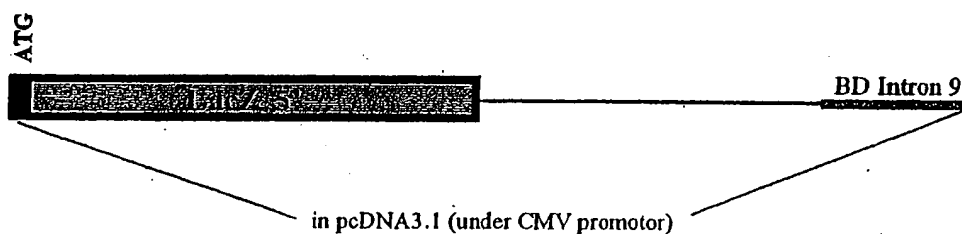


FIGURE 11

LacZ-PTM-3 (Intron 9 specific binding domain) and LacZ-PTM-4 (non specific binding domain) for establishing optimal trans-splicing conditions

Lac-PTM³



Lac-PTM⁴

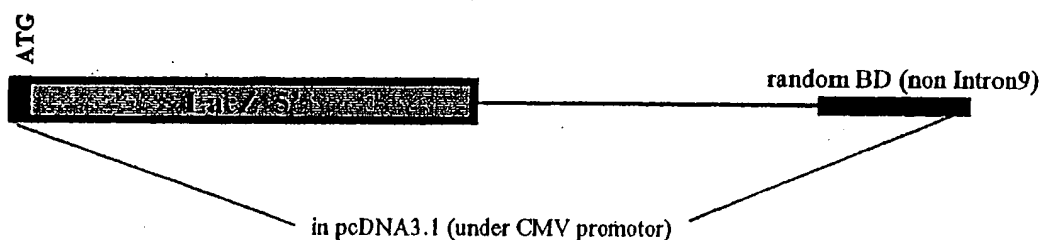


FIGURE 12

PLEC-PTM-5 for the introduction of the 1287ins3 mutation
in 293T cells

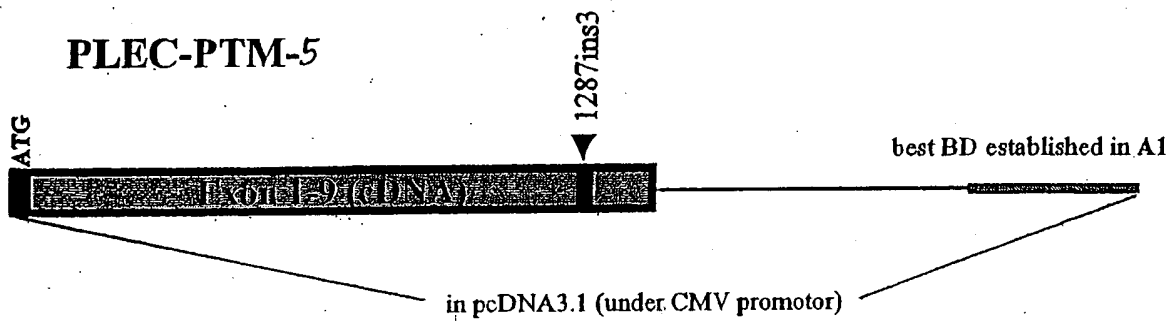


FIGURE 13

PLEC-PTM-6 for the repair of the 1287ins3 mutation
in plectin deficient patient cells

PLEC-PTM-6

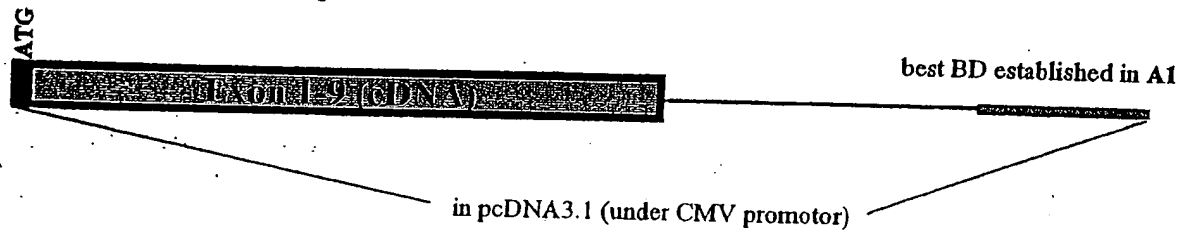


FIGURE 14A

Trans-splicing Strategy for Col17A1 Gene (GABEB/generalized atrophic benign epidermolysis bullosa)

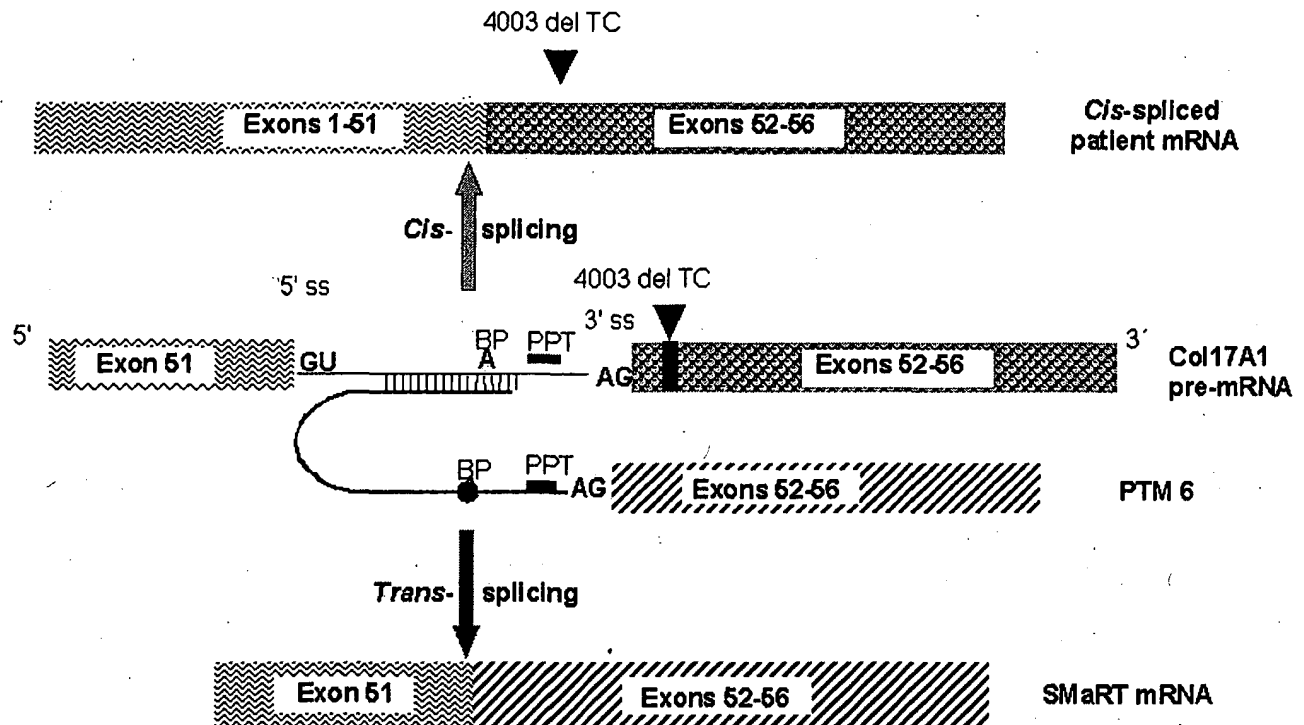
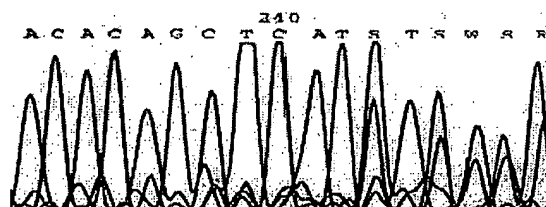
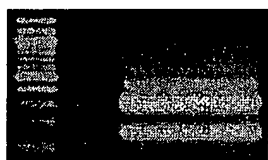


FIGURE 14B

Semi-nested RT-PCR with BPAG2- primer 51-1F, 53-1R and 52-1R

RT-PCR



TCGTCTCA - IV
TGTTCAGCA - III

F1
B1
C

FIGURE 14C

TOPO Cloning + Nla III digest

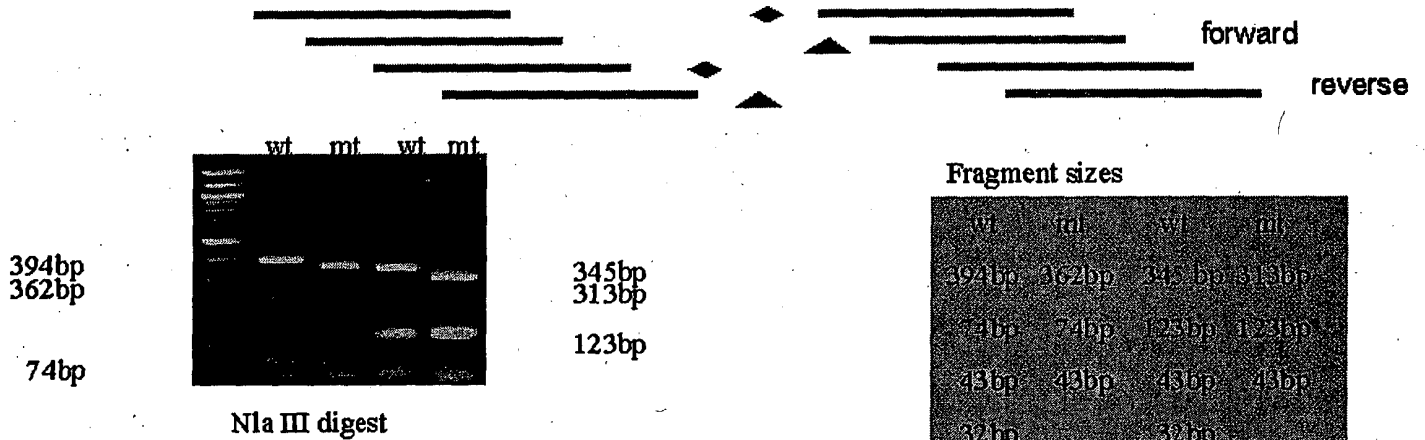


FIGURE 14D

Sequencing of mutant and
wildtype clones confirmed the
correct *trans*-splicing of PTM6
into GABEB cells

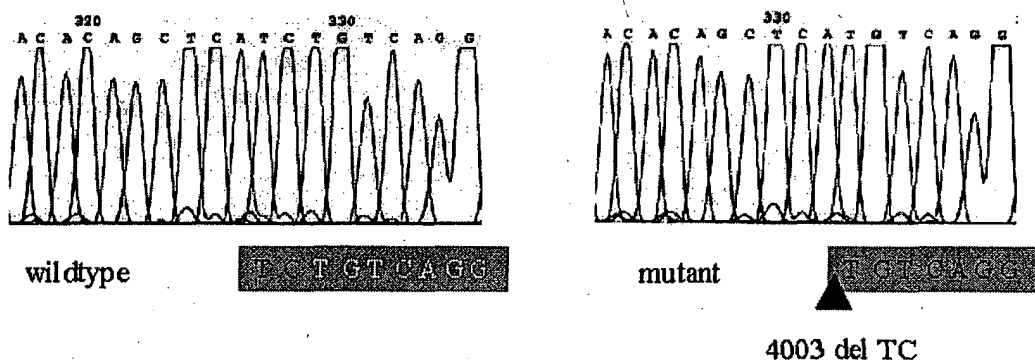


FIGURE 14E

Analysis of 100 clones

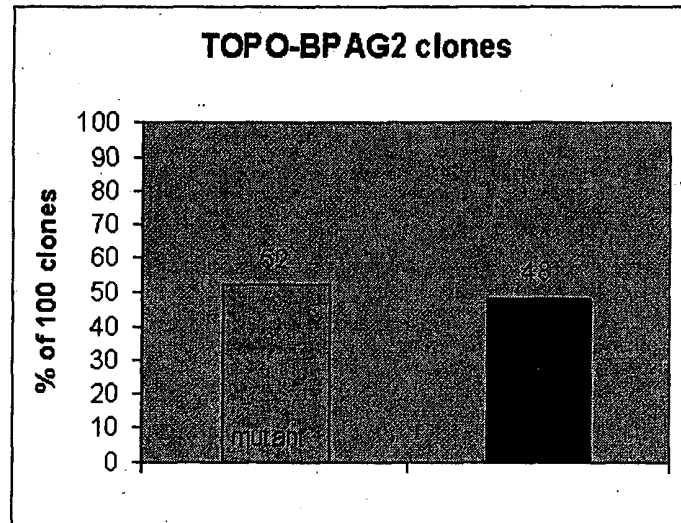


FIGURE 15

Immunofluorescence of PTM6- transfected GABEB cells

GABEB
non-transfected



GABEB
PTM6 transfected, 3 days

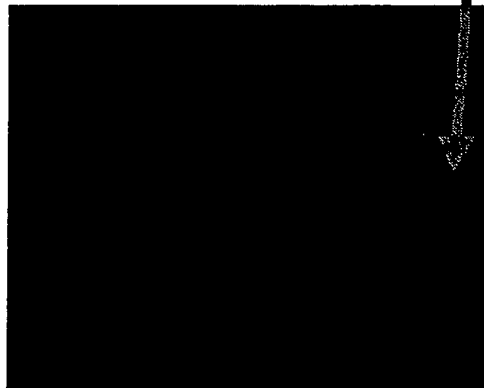
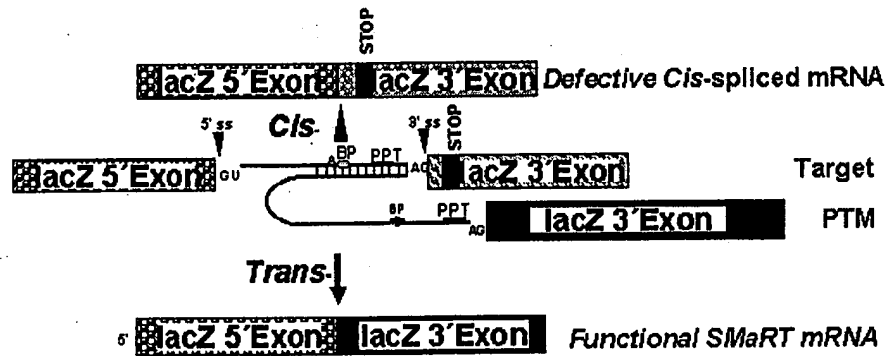


FIGURE 16A-B

Trans-splicing strategy for COL7A1 gene (Dystrophic epidermolysis bullosa)

A.



B.

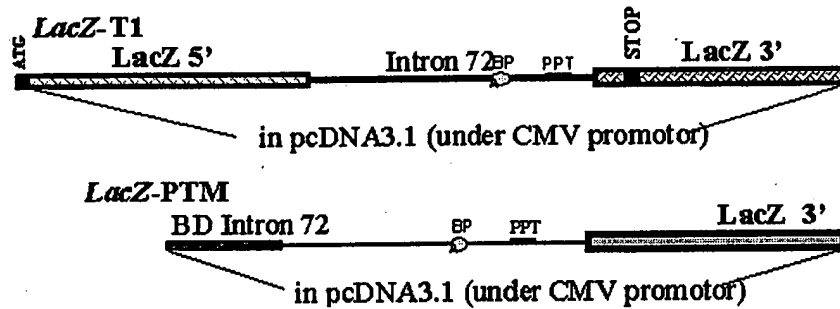


FIGURE 17

β -gal Assay of a Cotransfection of Col7 Target T1 and PTM 8, 9, 10 in 293T cells

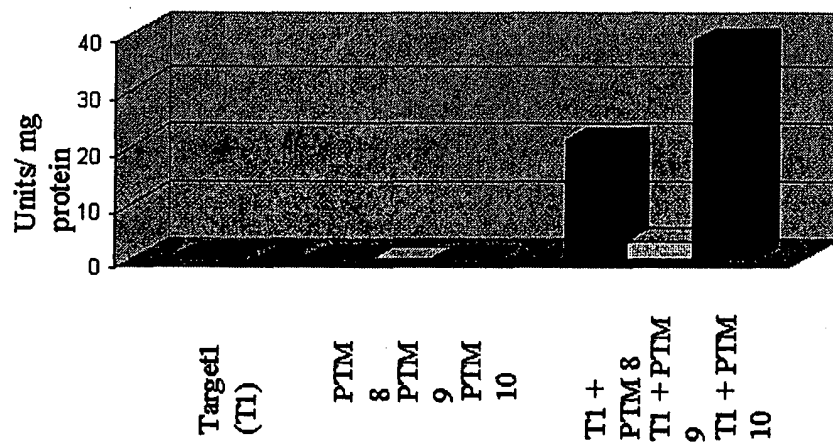
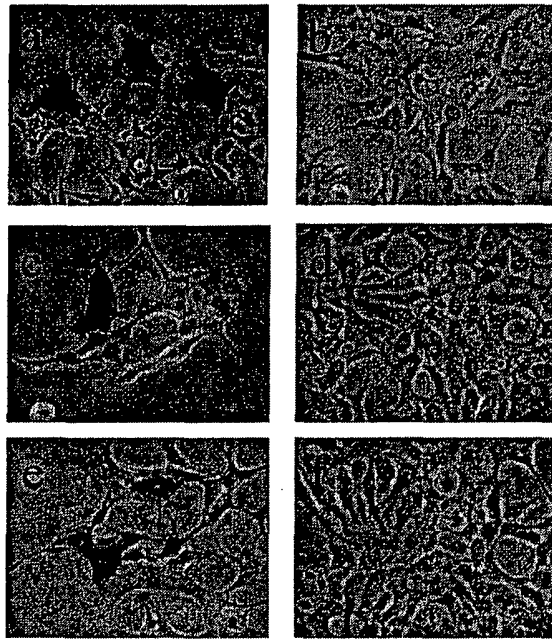


FIGURE 18

Beta-gal staining of Col7 PTM transfected human 293T cells



left panel: (a) Target + PTM8, (c) Target + PTM9, (e) Target + PTM10;
right panel: corresponding control PTM without Target.